UNITED STATES PATENT AND TRADEMARK OFFICE

A

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/606,909 | 06/29/2000 | Ronald J. Pettis | P-4901 | 7814 |

20583 7590 04/07/2005

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

| EXAMINER | |
|---|---|
| HAYES, MICHAEL J | |
| **ART UNIT** | **PAPER NUMBER** |
| 3763 | |

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

SP

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/606,909 | PETTIS ET AL. | |
| | Examiner | Art Unit | |
| | Michael J. Hayes | 3763 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-7,10-24 and 29* is/are pending in the application.

4a) Of the above claim(s) *17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,10-16 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election of claim 29 in the reply filed on 3/19/2004 is acknowledged.

Claims 17-24 are listed as withdrawn.

Claims 2-7, 10-16, and 29 are treated on the merits below.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29, 2-5, 10-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for delivering insulin and PTH, and similar hormones, the specification is not enabling for all drugs delivered at all pressure ranges to control all delivery flow rates. Applicant's disclosure does not support a claim dominating every drug and its delivery into a intradermal compartment. There is a lack of reasonable correlation between the disclosure and the broad scope of protection of the claims. Because of undue experimentation required to use the claimed method, these claims are rejected as not being enabled.

The experimentation is considered undue because biologic system have well recognized unpredictability, particularly with respect to drug effects on individuals, a large number of experiments are required to find the correct parameters to achieve the claimed method though the experimental methods are well known, and the lack of guidance in the specification.

Applicant's statement that experiments using various pressures combined with blood tests over a period of time (Applicant's data show approximately 6 hrs of experimentation per pressure value would be expected) along with various delivery sites on a patient's skin and repeating the same conditions except with subcutaneous injection would be required for each drug desired to be used in the claimed method. This would result in a very large number of experiments that would require an inordinate amount of time, and therefore are undue. Applicant provides guidance for one example with insulin and one example with PTH. This narrow disclosure is insufficient to support a method of delivering all drugs, at all pressures/flow rates, for any patient.

Applicant's specification at page 7, lines 21-23 acknowledges that the data demonstrates the method's efficacy for hormone drugs and "indicates that ID infusion may actually provide higher plasma levels for drugs that are susceptible to in vivo biological degradation or clearance." (emphasis added). Applicant's own uncertainty with respect to the method's efficacy for other drugs shows the unpredictability of the disclosed method.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29, 2, 3, 5-7, and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by GROSS et al. (US Patent No. 5,848,991). Gross discloses a method of delivering insulin and hormones intradermally (3:40-41; 6:56 - 7:20) using a single needle with an outlet at a depth of 250 μm - 2mm in a controlled manner based on needle diameter (4:10-35). The plasma profile would be inherently similar to, but higher as compared to subcutaneous injection. Because Applicant argues that the needle length and enough pressure to control delivery are the essential limitations required to achieve the claimed method these limitations found in Gross would inherently allow the method disclosed in Gross to achieve a higher Cmax and AUC as compared to subcutaneous injection.

Claims 29, 4, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by GANDERTON et al. (US Patent No. 3,814,097). Ganderton discloses injecting a substance through multiple needles with a zero exposed height (2:37-55) with an outlet at 1000 μm (2:55-60). See fig. 1. The plasma profile is inherently similar to, but higher as compared to subcutaneous injection. Applicant states that the needle length and enough pressure to control flow are the essential limitations required to inherently achieve the claimed method.

Claim 29, 2, 3, 5, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by AUTRET et al. (Therapie 1991; 46:5-8). Autret discloses intradermal injection of a hormone that results in a pharmacokinetic profile similar to subcutaneous delivery, but with a higher plasma level and area under the curve (AUC) at about 1 hr. (See fig. 1 and results section)

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29, 2, 3, 5-7, 10-13, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross in view of PURI (*An investigation of the intradermal route as an effective means of immunization for microparticulate vaccine delivery systems*) or D'Antonio et al. (US Patent No. 6,056,716). If the claimed method of intradermal delivery disclosed by Gross is not inherent it would have been obvious to one of ordinary skill in the art to deliver drugs at particular pressures and flow rates to achieve higher Cmax and AUC than subcutaneous injection. Puri and D'Antonio disclose that intradermal injections give much greater Cmax values than subcutaneous. The prior art disclosures suggest a greater Cmax and AUC. (see Puri, pgs. 2609-2610, and D'Antonio col. 29, lines 3-9). It would have been obvious to one of ordinary skill in the art at the time of the invention to use the teachings of Puri or D'Antonio in the method of Gross in order to more effectively treat patients and save drug costs.

### *Response to Arguments*

Applicant states that Autret does not recognize higher maximum plasma concentration and bioavailability. The examiner disagrees because the data presented by Autret shows a higher Cmax (See fig. 1). Also Autret shows a higher AUC at experimental times around 1hr. The difference in Autret's recognition and Applicant's of their own data appears to be based on

differing statistical analysis; however Applicant has not claimed any results with respect to a particular statistical significance.

The role of pressure is not consistent in Applicant's arguments. Pressure is acknowledged as a critical feature in the first paragraph on pg. 7 of remarks received 1/06/05, but then Applicant states "Nor is the absolute value at which pressure is applied critical to the claimed invention." (3rd paragraph of remarks received 1/06/05). Since pressure values determine the flow rate it appears from the specification that it is a critical feature of the claimed method. Applicant should reconcile their statements concerning pressure values.

Applicant has not showed any data to support their statement that ID delivery would not inherently result in a higher Cmax and AUC, and therefore have not met their burden in arguing against inherency. Applicant arguments concerning avoiding leakage or excessive weal formation at the skin surface does not apply to delivering to the intradermal compartment. Delivery to the intradermal compartment requires that the drug is delivered to this volume, not that some leaks at the skin surface. Therefore it appears that when a drug is delivered to the intradermal compartment it inherently results in a higher Cmax and AUC.

The declaration submitted under 37 CFR 1.132 has been considered, but does not provide data or facts sufficient to withdraw the present rejections. There is no data or facts presented that show delivery to the intradermal compartment does not inherently result in higher Cmax and AUC. The discussed fact that pressure is applied to deliver drugs (disclosed in the specification) to the intradermal compartment to give higher Cmax and AUC does not refute the inherency rejection. Showing only data where the desired result was achieved does not meet Applicant's burden that the results are not inherent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Hayes at (703) 305-5873. The examiner can usually be reached Monday -Thursday, 7:00-4:30, and on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nick Lucchesi, can be contacted at (703) 308-2698. The fax number for submitting official papers is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mjh
4 April 2005

MICHAEL J. HAYES
PRIMARY EXAMINER